**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION**
**DECISION SUMMARY**
**ASSAY ONLY TEMPLATE**

**A. 510(k) Number:**
k120615

**B. Purpose for Submission:**
Modification of the previously cleared Cholestech LDX (k901900, k932727); the introduced change is to include ROM software upgrade from v3.30 to v3.41 for correction of humidity interference.

**C. Measurand:**
Total Cholesterol (TC)
Triglycerides (TRG)
Glucose (GLC)
High density cholesterol (HDL)
Low-density lipoprotein (LDL) – by calculation

**D. Type of Test:**
Quantitative

**E. Applicant:**
Alere San Diego, Inc.

**F. Proprietary and Established Names:**
Alere Cholestech LDX® Analyzer and Alere Cholestech Lipid Profile•GLU Cassette

**G. Regulatory Information:**

1. Regulation section:
   21 CFR § 862.1345, Glucose test system.
   21 CFR § 862.1175, Cholesterol (total) test system
   21 CFR § 862.1475, Lipoprotein test system.
   21 CFR § 862.1705, Triglyceride test system.
   21 CFR § 862.2160, Analyzer, Chemistry (photometric, discrete), For Clinical Use

2. Classification:
   Class II; Class I, meets limitation for exemption per 21 CFR 862.9(c)(4) and (9); Class I

3. Product code:
   CGA
   CHH
   LBS
   JGY
   JJE

4. Panel:
   Clinical Chemistry (75)

**H. Intended Use:**

1. Intended use(s):
   See Indication(s) for use below.

2. Indication(s) for use:
   The Alere Cholestech LDX® System is a small, portable analyzer and test cassette system. The System is for in vitro diagnostic use only. The Lipid Profile•GLU Cassette is for the quantitative determination of total cholesterol, HDL (high-density lipoprotein) cholesterol, triglycerides and glucose in whole blood. A TC/HDL (total cholesterol/HDL cholesterol ratio and estimated values for LDL (low-density lipoprotein) and non-HDL cholesterol are calculated by the Alere Cholestech LDX® Analyzer.
   - Cholesterol measurements are used in the diagnosis and treatment of disorders involving excess cholesterol in the blood and lipid and lipoprotein metabolism disorders.
   - HDL (lipoprotein) measurements are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis, and various liver and renal diseases.
   - Triglyceride measurements are used in the diagnosis and treatment of patients with diabetes mellitus, nephrosis, liver obstruction, other diseases involving lipid metabolism, or various endocrine disorders.
   - Glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia, and idiopathic hypoglycemia, and of pancreatic islet cell carcinoma.

3. Special conditions for use statement(s):
   For prescription use.

   The sponsor states the following limitations in their package insert (PI):

   "If the measured value of TRG is >400 mg/dL (>4.51 mmol/L), the LDX displays "N/A" for the LDL estimate.

   The sponsor certification for CRMLN was verified with the sponsor and confirmed at http://www.cdc.gov/labstandards/crmln_clinical.html.

4. Special instrument requirements:
   Alere Cholestech LDX Analyzer.

**I. Device Description:**

The Alere Cholestech LDX® System is a small, portable analyzer and test cassette

system. The System is for in vitro diagnostic use only. The Analyzer uses reflectance photometry (the amount of light reflected from a solid surface) to measure the amount of substances in blood. The analyzer measures color changes of the four reagent pads. The amount of color formed is converted by the analyzer to a concentration and the results are shown on the liquid crystal display (LCD) screen. The assays for use on the Analyzer include total cholesterol (TC), high-density lipoprotein cholesterol (HDL), triglycerides (TRG), glucose (GLU), and by calculation, low-density lipoprotein (LDL).

The modification that is the subject of this submission is with regards to a software upgrade. The software used to run the Alere Cholestech LDX® Analyzer is provided as an upgradable Read Only Memory (ROM) Pack that connects to the Analyzer on the back panel. The ROM pack upgrade includes a humidity sensor attached to the front casing of the ROM pack and is backwards compatible to all Alere Cholestech LDX® Analyzers. The sensor is connected to the existing circuit board.

## J. Substantial Equivalence Information:

1. Predicate device name(s):
   Alere Cholestech LDX® Lipid Monitoring System v.3.30

2. Predicate 510(k) number(s):
   k901900
   k932727

3. Comparison with predicate:

| **Software Version Comparison Similarities** | | |
|---|---|---|
| Item | New Device Alere Cholestech LDX® System, ROM pack version v.3.41 | Predicate Alere Cholestech LDX® System, ROM pack version v.3.30 |
| Intended Use | For the quantitative determination of total cholesterol, HDL (high-density lipoprotein) cholesterol, triglycerides and glucose in whole blood. A TC/HDL (total cholesterol/HDL cholesterol ratio and estimated values for LDL (low-density lipoprotein) and non-HDL cholesterol are calculated by the Alere Cholestech LDX® | Same |

| Software Version Comparison<br>Similarities | | |
|---|---|---|
| Item | New Device<br>Alere Cholestech LDX® System, ROM pack version v.3.41 | Predicate<br>Alere Cholestech LDX® System, ROM pack version v.3.30 |
| | Analyzer | |
| Analytes Available | TC<br>HDL<br>TRG<br>GLU | Same |

| Differences | | |
|---|---|---|
| Item | New Device<br>Alere Cholestech LDX® System, ROM pack version v.3.41 | Predicate<br>Alere Cholestech LDX® System, ROM pack version v.3.30 |
| | v.3.41 | v.3.30 |
| Humidity Sensor | included on ROM pack | not included |
| Humidity Correction Factor | Applied to assay test results | Not applied to any assay results |
| Matrix | Whole blood | Whole blood, serum and plasma |

**K. Standard/Guidance Document Referenced (if applicable):**
Not applicable

**L. Test Principle:**
The Alere Cholestech LDX® System combines enzymatic methodology and solid-phase technology to measure total cholesterol, HDL cholesterol, triglycerides and glucose. Samples used for testing can be whole blood from a fingerstick (collected in a lithium heparin-coated capillary tube) or venipuncture. The sample is applied to an Alere Cholestech LDX® cassette. The cassette is then placed into the Alere Cholestech LDX® Analyzer where a unique system on the cassette separates the plasma from the blood cells. A portion of the plasma flows to the right side of the cassette and is transferred to both the total cholesterol and triglyceride reaction pads. Simultaneously, plasma flows to the left side of the cassette where the low- and very low-density lipoproteins (LDL and VLDL) are precipitated with dextran sulfate (50,000 MW) and magnesium acetate precipitating reagent.[5] The filtrate, containing both glucose and HDL cholesterol, is transferred to both the glucose and HDL cholesterol reaction pads.

The Alere Cholestech LDX® Analyzer measures total cholesterol and HDL cholesterol by an enzymatic method based on the method formulation of Allain et al,[5] and Roeschlau.[6] Cholesterol esterase hydrolyzes the cholesterol esters in the filtrate or plasma to free cholesterol and the corresponding fatty acid. Cholesterol oxidase, in the

presence of oxygen, oxidizes free cholesterol to cholest-4-ene-3-one and hydrogen peroxide. In a reaction catalyzed by horseradish peroxidase, the peroxide reacts with 4-aminoantipyrine and N-ethyl-N-sulfohydroxypropyl-m-toluidine, sodium salt (TOOS) to form a purple-colored quinoneimine dye proportional to the total cholesterol and HDL cholesterol concentrations of the sample.

The Alere Cholestech LDX® Analyzer measures triglycerides by an enzymatic method based on the hydrolysis of triglycerides by lipase to glycerol and free fatty acids. Glycerol, in a reaction catalyzed by glycerol kinase, is converted to glycerol-3-phosphate. In a third reaction, glycerol-3-phosphate is oxidized by glycerol phosphate oxidase to dihydroxyacetone phosphate and hydrogen peroxide.[7] The color reaction utilizing horseradish peroxidase is the same as for the total cholesterol and HDL cholesterol.

The Alere Cholestech LDX® Analyzer measures glucose by an enzymatic method that uses glucose oxidase to catalyze the oxidation of glucose to gluconolactone and hydrogen peroxide. The color reaction utilizing horseradish peroxidase is the same as that for total cholesterol, HDL cholesterol and triglycerides. The resultant color in all the reactions is measured by reflectance photometry.

A brown (magnetic) stripe on each cassette contains the calibration information required for the Alere Cholestech LDX® Analyzer to convert the reflectance reading (% R) to the total cholesterol, HDL cholesterol, triglycerides and glucose concentrations.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:
   a. *Precision/Reproducibility:*
   Analytical performance of these devices was reviewed under k901900, k912136, k914469, k922612, k932727, k914033, k905296 and k904082.

   b. *Linearity/assay reportable range:*
   Established in original submissions k901900, k912136, k914469, k922612, k932727, k914033, k905296 and k904082.

Measuring range:

| Analyte | Measuring Range | For results outside the measuring range, the LDX displays: | |
|---|---|---|---|
| | mg/dL (mmol/L) | Low | High |
| TC | 100 – 500 (2.59 –12.9) | <100 mg/dL (<2.59 mmol/L) | >500 mg/dL (>12.9 mmol/L) |
| HDL | 15 –100 (0.39 – 2.59) | <15 mg/dL (<0.39 mmol/L) | >100 mg/dL (>2.59 mmol/L) |
| TRG | 45 – 650 (0.51– 7.34) | <45 mg/dL (<0.51 mmol/L) | >650 mg/dL (>7.34 mmol/L) |

| | | | |
|---|---|---|---|
| GLU | 50 – 500 (2.78 – 27.8) | <50 mg/dL (<2.78 mmol/L) | >500 mg/dL (>27.8 mmol/L) |

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
Established in original submissions k901900, k912136, k914469, k922612, k932727, k914033, k905296 and k904082.

d. *Detection limit:*
Established in original submissions k901900, k912136, k914469, k922612, k932727, k914033, k905296 and k904082.

e. *Analytical specificity:*
Established in original submissions k901900, k912136, k914469, k922612, k932727, k914033, k905296 and k904082.

**Humidity Interference**
This software upgrade incorporates humidity sensor and applies humidity correction factors from a look up table to the result from the assay algorithm. The sponsor carried out the humidity interference validation studies with their modified device (which includes ROM v3.41 software upgrade with humidity sensor and humidity correction factors) across the 20-80% (20%, 30%, 40%, 50%, 60%, 70, 80% RH) relative humidity range against their predicate device at nominal 50% relative humidity. The sponsor tested whole blood samples across claimed measuring range for each of the analytes and showed that the performance characteristics are substantially equivalent to the predicate device. The sponsor also provided precision studies for each of the claimed analytes and showed that the precision of modified device meets the sponsor's pre-specified acceptance criteria of the predicate device.

f. *Assay cut-off:*
Established in original submissions k901900, k912136, k914469, k922612, k932727, k914033, k905296 and k904082.

2. Comparison studies:
   a. *Method comparison with predicate device:*
   Established in original submissions k901900, k912136, k914469, k922612, k932727, k914033, k905296 and k904082.

   b. *Matrix comparison:*
   Established in original submissions k901900, k912136, k914469, k922612, k932727, k914033, k905296 and k904082.

3. Clinical studies:
   a. *Clinical Sensitivity:*
   Not applicable

*b. Clinical specificity:*
Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):
Not applicable

4. Clinical cut-off:
Not applicable

5. Expected values/Reference range:

**Cholesterol and Triglycerides**

The National Heart, Lung and Blood Institute issued the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) in May, 2001.[1] The ATP III report presents NCEP's updated clinical guidelines for cholesterol testing and management and describes the following classifications for cholesterol and triglyceride testing:

| Analyte | mg/dL | mmol/L | Classification |
|---|---|---|---|
| LDL cholesterol | <100 | <2.59 | Optimal |
| | 100 –129 | 2.59 – 3.34 | Near optimal/above optimal |
| | 130 –159 | 3.36 – 4.11 | Borderline high |
| | 160 –189 | 4.14 – 4.89 | High |
| | ≥190 | ≥4.91 | Very high |
| Total cholesterol | <200 | <5.18 | Desirable |
| | 200 – 239 | 5.18 – 6.19 | Borderline high |
| | ≥240 | ≥6.22 | High |
| HDL cholesterol | <40 | <1.03 | Low |
| | ≥60 | ≥1.55 | High |
| Triglycerides | <150 | <1.69 | Normal |
| | 150 –199 | 1.69 – 2.25 | Borderline high |
| | 200 – 499 | 2.26 – 5.64 | High |
| | ≥500 | ≥5.65 | Very high |

The ATP III identified HDL cholesterol levels below 40 mg/dL (1.03 mmol/L) as associated with increased risk of coronary heart disease (CHD) in men and women.[1] A high HDL cholesterol level greater than or equal to 60 mg/dL (1.55 mmol/L) is protective and decreases CHD risk.

**TC/HDL Ratio**

A ratio of 4.5 or less is desirable. A ratio greater than 6.0 suggests a high risk of CHD.[2]

**Non-HDL**

ATP III identifies non-HDL cholesterol (total cholesterol minus HDL cholesterol) as a secondary target of therapy in persons with high triglycerides (≥200 mg/dL).

The goal for non-HDL cholesterol in persons with high serum triglycerides can be set at 30 mg/dL higher than that for LDL cholesterol on the premise that a VLDL cholesterol level ≤30 mg/dL is normal.[1]

**Glucose**

The American Diabetes Association has identified categories of increased risk for diabetes based upon glucose[4]:

- Fasting plasma glucose (FPG) 100 -125 mg/dL (5.6 -6.9 mmol/L); impaired fasting glucose
- 2-hr plasma glucose in the 75-g oral glucose tolerance test (OGTT) 140 -199 mg/dL (7.8 -11.0 mmol/L); impaired glucose tolerance

For these tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately greater at higher ends of the range.

The American Diabetes Association has criteria for the diagnosis of diabetes mellitus based upon glucose[4]:

- FPG ≥126 mg/dL (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 hr.
- 2-h plasma glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.
- In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).

In the absence of unequivocal hyperglycemia, diagnosis should be confirmed by repeat testing. When screening for diabetes, any abnormal glucose result should be referred to a physician for further follow-up.

**References:**


1. Expert Panel on Detection, Evaluation, and Treatment of High Cholesterol in Adults. Executive summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001;285:2486-97.
2. Castelli WP, Abbott RD, McNamara PM. Summary estimates of cholesterol used to predict coronary heart disease. *Circulation* 1983;67:730-4.
3. Kinosian B, Glick H, Garland G. Cholesterol and coronary heart disease: predicting risks by levels and ratios. *Ann Intern Med* 1994;121:641-7.
4. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2013;36(Suppl.1):S67-74.
5. Allain CC, Poon LS, Chan CS, Richmond W, Fu PC. Enzymatic determination of total serum cholesterol. *Clin Chem* 1974;20:470-5.
6. Roeschlau P, Bernt E, Gruber W. Enzymatische bestimmung des gesamtcholesterins im serum. *Z Klin Chem Klin* Biochem 1974;12:226.
7. Fossati P, Prencipe L. Serum triglycerides determined colorimetrically with an enzyme that produces hydrogen peroxide. *Clin Chem* 1982;28:2077-80.

**N. Instrument Name:**

Alere Cholestech LDX® Analyzer

**O. System Descriptions:**

1. Modes of Operation:
   The instrument identifies the assay by reading the magnetic stripe located on each of the assay cassette. The magnetic stripe contains the test names, instructions to the analyzer for running the tests on the cassette, and calibration information for converting the color reading to test concentration.

2. Software:
   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes ___X___ or No _____

3. Specimen Identification:
   There is no sample identification function with this device.

4. Specimen Sampling and Handling:
   **Sample Type:**
   Fingerstick or venous whole blood (used within 30 minutes) samples.

   **Sample Requirement:**
   - Sample Volume: 40 µL of whole blood.

   **Fingerstick whole blood:**
   - Collect the sample from a fingerstick into an Alere Cholestech LDX® 40 µL Capillary Tube.
   - Place the blood into the cassette within 8 minutes after collection.

   **Venous whole blood:**
   - Collect blood into a green-top tube (heparin anticoagulant) and use a pipette tip to place blood into the cassette.

5. Calibration:
   No calibration is performed by the user. Test information is encoded on the brown stripe of the cassette. The brown magnetic stripe is read by the Alere Cholestech LDX® Analyzer each time a cassette is run.

6. Quality Control:
   Liquid Level 1 and Level 2 controls for the Alere Cholestech LDX® System are available.
   Controls should be tested:
   • With each new lot of cassettes;
   • With every new shipment of cassettes, even if the lot has been received

previously;
• When reagents may have been stored or handled in a way that can degrade their performance;
• As otherwise required by your laboratory's standard quality control procedures;
• As otherwise required by federal, state and local guidelines.

**P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:**

**Q. Proposed Labeling:**
The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

**R. Conclusion:**
The submitted information in this premarket notification is complete and supports a substantial equivalence decision.